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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,403	09/01/2006	Nobuhiko Fushimi	Q96347	9581

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EXAMINER	
LAU, JONATHAN S	
ART UNIT	PAPER NUMBER
1623	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,403	FUSHIMI ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2008 and 30 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-20 and 25-29* is/are pending in the application.

4a) Of the above claim(s) *17-20 and 25-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 5-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 27 Aug 2008, in which claims 4 is amended to correct its dependency, claim 5 is amended to change the scope and breadth of the claim, and claim 2 is canceled; and Applicant's Supplemental Amendment, filed 30 Sep 2008, in which claim 4 is canceled and claim 5 is amended to change the scope and breadth of the claim as per Applicant's Amendment, filed 27 Aug 2008.

Applicant's Supplemental Amendment, filed 30 Sep 2008, will be entered because the supplemental reply is clearly limited to cancellation of a claim(s).

This application is the national stage entry of PCT/JP05/04152, filed 03 Mar 2005; and claims benefit of foreign priority document JAPAN 2004-61429, filed 04 Mar 2004; currently an English language translation of this foreign priority document is of record.

Claims 1, 3, 5-20 and 25-29 are pending in the current application. Claims 17-20 and 25-29, drawn to non-elected inventions, are withdrawn. Claim 3, withdrawn as drawn to non-elected species, is rejoined.

Election/Restrictions

The First and Second election of species requirement, detailed in the Office Action mailed 03 Jan 2008, is withdrawn.

Claim 3, drawn to non-elected species, is rejoined.

Rejections Withdrawn

Applicant's Amendment, filed 30 Sep 2008, with respect to claims 1-2 and 4-16 rejected under 35 U.S.C. 103(a) as being unpatentable over Imamura et al. (WIPO Publication WO2004/080990, published 23 Sep 2004, of record) in view of Shell (US Patent 5,582,837, issued 10 Dec 1996, of record) has been fully considered and is persuasive, as claims 2 and 4 are canceled and foreign priority is perfected by filing of an English language translation of foreign priority document JAPAN 2004-61429, which provides support for instant claims 1, 3 and 5-16 with a foreign priority date of 04 Mar 2004. Therefore WIPO Publication WO2004/080990, published 23 Sep 2004 in Japanese, is not prior art under 35 U.S.C. 102(a) or (e).

This rejection has been **withdrawn**.

Applicant's Remarks, filed 30 Sep 2008, with respect to claims 1-2 and 4-16 rejected under 35 U.S.C. 103(a) as being unpatentable over Ellsworth et al. (US Patent 6,414,126, issued 02 Jul 2002, of record) in view of Bedell et al. (J. Org. Chem., 1962, 27, p2026-2031, of record) and further in view of Shell (US Patent 5,582,837, issued 10 Dec 1996, of record) has been fully considered and is persuasive, as claims 2 and 4 are canceled and Applicant's remarks that Ellsworth et al. in view of Bedell et al. and further

in view of Shell does not provide sufficient guidance to a person of ordinary skill in the art to arrive at the presently claimed invention wherein the glycoside is attached to the 5-membered ring of the fused heterocycle according to the presently claimed invention with a reasonable expectation of success is found to be persuasive.

This rejection has been **withdrawn**.

The following are new grounds of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended Claims 1, 3 and 5-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Amended claims 1, 3, 5-9 recite "a prodrug thereof". Amended claims 10-16 depend directly or indirectly from claims 1, 8 and 9, and incorporate all limitations therein.

The recitation, "prodrug", is seen to be merely functional language, defining by function a compound that must undergo chemical conversion by metabolic processes before becoming an active pharmacological agent.

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

Thus, Applicants functional language at the points of novelty fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the

more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, as discussed above in *University of California v. Eli Lilly and Co*. Hence, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the pharmaceutical compositions herein.

Amended Claims 1, 3 and 5-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of Example 1, 2 and 3 as an agent for the treatment a disease associated with hyperglycemia selected from the group consisting of diabetes, impaired glucose tolerance, diabetic complications, obesity, hyperinsulinemia, hyperlipidemia, hypertriglyceridemia, atherosclerosis, hypertension and edema; does not reasonably provide enablement for all compounds of general formula (I) as an agent for the inhibition of postprandial hyperglycemia, prevention of a disease associated with hyperglycemia, treatment a disease associated with hyperglycemia selected from the group consisting of hypercholesterolemia, congestive heart failure, hyperuricemia and gout, or for inhibition of advancing impaired glucose tolerance into diabetes in a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: A compound of general formula (I) as defined in claim 1, and pharmaceutical compositions thereof, having an intended use as an agent for the treatment a disease associated with hyperglycemia selected from the group consisting of diabetes, impaired glucose tolerance, diabetic complications, obesity, hyperinsulinemia, hyperlipidemia, hypertriglyceridemia, atherosclerosis, hypertension and edema; as an agent for the inhibition of postprandial hyperglycemia, prevention of a disease associated with hyperglycemia, treatment a disease associated with hyperglycemia selected from the group consisting of hypercholesterolemia, congestive heart failure, hyperuricemia and gout, or for inhibition of advancing impaired glucose tolerance into diabetes in a subject.

The state of the art: Handlon (Expert Opin. Ther. Patents, 2005, 15(11), p1531-1540, cited in PTO-892), published after the instant filing date, reviews compounds having activity as inhibitors of SGLT2 (page 1531, paragraph 1). Handlon discloses the use of SGLT2 inhibitors to treat diabetes characterized by insulin resistance and

hyperglycemia, which can lead to damage of the retina, kidney and nerve tissue. Handlon discloses diabetic complications such as heart disease and stroke (page 1533, left column, paragraph 2). Handlon discloses SGLT2 inhibitors are capable of use to treat obesity and decrease triglycerides (page 1538, right column paragraph 2). Handlon discloses a specific compounds that have biological activity (page 1536, figure 3).

Ellsworth et al. (Bioorganic and Medicinal Chemistry Letters, 2008, 18, p4770-4773, cited in PTO-892), published after the instant filing date, discloses structural-activity relationships for a series of C-arylglucoside inhibitors of SGLT2, demonstrating that variation of the structure of the compound can lead to significant loss of SGLT2 activity (page 4771, left column, paragraph 1 and right column, paragraph 4).

Dudash Jr. et al. (Bioorganic and Medicinal Chemistry Letters, 2004, 14, p5121-5125, cited in PTO-892) discloses structural-activity relationships for a series of O-linked glycosylated dihydrochalcones that possess activity as SGLT2 inhibitors, demonstrating varying the substituents can lead to significant loss of SGLT2 activity (page 5124, left column, paragraph 1 and right column, paragraph 2).

Vemula et al. (J. Pharma. Exp. Ther., 2008, accessed online at http://jpet.aspetjournals.org, cited in PTO-892), published after the instant filing date, discloses SGLT inhibitors are capable of use as an agent for treatment of edema (page 3, abstract).

Ellsworth et al. (US Patent 6,414,126, of record), the '126 Patent hereafter, discloses C-arylglucoside inhibitors of SGLT2 are capable of use as an agent for

treating or delaying the progression or onset of diabetes, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, atherosclerosis or hypertension (column 73, claim 26).

The ordinary definition of prevention of a disease encompasses making impossible said disease (definition of prevent, WordNet, cited in PTO-892). No prior art discloses or teaches making the above recited diseases impossible.

The ordinary definition of inhibition encompasses completely blocking an action or function, as well as limiting or decreasing an action or function (definition of inhibit, WordNet, cited in PTO-892). No prior art discloses or teaches completely blocking postprandial hyperglycemia or completely blocking advancing impaired glucose tolerance into diabetes in a subject.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: As taught in Handlon, Ellsworth et al., and Dudash Jr. et al., variation of the structure of the compound can lead to significant loss of SGLT2 activity. Therefore the claimed invention is unpredictable.

The Breadth of the claims: The scope of the claims is infinite. Any possible combination of chemical groups as defined in general formula (I) could potentially be used as the compound of general formula (I).

The amount of direction or guidance presented: The specification speaks generally about the use of the compounds of the instant invention as SGLT inhibtors (page 6, paragraph 1). However, guidance is not given for use as an agent for the

inhibition of postprandial hyperglycemia, prevention of a disease associated with hyperglycemia, treatment a disease associated with hyperglycemia selected from the group consisting of hypercholesterolemia, congestive heart failure, hyperuricemia and gout, or for inhibition of advancing impaired glucose tolerance into diabetes in a subject. No limiting definition of prevention or inhibition is provided.

The presence or absence of working examples: The only working examples provided are for the inhibition of SGLT in an in vitro system using the compounds of example 1, 2 and 3.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as organic compounds and pharmaceutical agents. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the invention with the full range of all possible compounds and intended uses beyond those known in the art, (such as the c-aryl glycosides capable of treating specific disorders disclosed in the '126 Patent) one skilled in the art would undertake a novel and extensive research program in to the pharmacological activity of an infinite scope of compounds. Because this research would have to be exhaustive, and because it would involve such a wide and unpredictable scope of compounds and disorders, it would constitute an undue and unpredictable experimental burden.

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims, Applicants fail to provide information sufficient to practice the claimed invention for all possible compounds of general formula (I) as an agent for the inhibition of postprandial hyperglycemia, prevention of a disease associated with hyperglycemia, treatment a disease associated with hyperglycemia selected from the group consisting of hypercholesterolemia, congestive heart failure, hyperuricemia and gout, or for inhibition of advancing impaired glucose tolerance into diabetes in a subject.

Conclusion

No claim is found to be allowable.

This Office Action details new grounds of rejection not necessitated by Applicant's Amendment. Accordingly, this Office Action is Non-Final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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